

Application No. 09/920,435
Filed: August 1, 2001
Group Art Unit: 1639

AMENDMENTS TO THE CLAIMS

Please amend claims 3 and 13 to read as follows:

Claim 1. (Original) A method of screening a natural sample for an affinity ligand that binds to a protein target, comprising:

- (1) mixing a protein target and a natural sample in solution to form a reaction mixture;
- (2) incubating the reaction mixture under conditions allowing complex formation by the target and any target-binding ligand present in the sample;
- (3) passing the reaction mixture through a first size-exclusion medium that removes from the reaction mixture any small molecular weight compounds each having a molecular weight less than a first preset value;
- (4) subjecting the size-excluded reaction mixture from step (3) to conditions promoting dissociation of any ligand/target complex into free ligand and free target; and
- (5) passing the reaction mixture resulting from step (4) through a second size exclusion medium that removes from the reaction mixture any molecule larger than a second preset value.

Claim 2. (Original) The method of claim 1, wherein the first size-exclusion medium removes molecules having a molecular weight of about 2,000 daltons or less.

Claim 3. (Currently Amended) The method of claim 1, wherein the first size-exclusion medium removes molecules having a molecular weight of about 1,500 daltons or less.

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Claim 4. (Original) The method of claim 1, wherein the first size-exclusion medium comprises a gel filtration or size exclusion HPLC column.

Claim 5. (Original) The method of claim 1, wherein step (4) comprises adding to the size-excluded mixture from step (3), a solution comprising an organic solvent and an organic acid.

Claim 6. (Original) The method according to claims 1, 4, or 5, wherein the second size-exclusion medium comprises an ultrafiltration membrane.

Claim 7. (Original) The method according to claims 1, 4, or 5, wherein the second size-exclusion medium removes from the reaction mixture, molecules having a molecular weight of about 10,000 daltons or more.

Claim 8. (Original) The method according to claims 1, 4, or 5, wherein the second size-exclusion medium removes from the reaction mixture, molecules having a molecular weight of about 3,000 daltons or more.

Claim 9. (Original) The method according to claims 1, 4, or 5, wherein the second size-exclusion medium removes from the reaction mixture, molecules having a molecular weight of about 2,000 daltons or more.

Claim 10. (Original) The method of claim 6, wherein the ultrafiltration membrane removes from the reaction mixture,

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molecules having a molecular weight of about 10,000 daltons or more.

Claim 11. (Original) The method of claim 6, wherein the ultrafiltration membrane removes from the reaction mixture, molecules having a molecular weight of about 3,000 daltons or more.

Claim 12. (Original) The method of claim 6, wherein the ultrafiltration membrane removes from the reaction mixture, molecules having a molecular weight of about 2,000 daltons or more.

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Claim 13. (Currently Amended) The method according to ~~claims 1, 4, or 5~~ claim 21, further comprising:

(7) comparing the analytical results of step (6) with a reference standard.

Claim 14. (Original) The method of claim 13, wherein the reference standard comprises the analytical results of subjecting either a sample of the protein target alone or a mixture of the protein target with a non-target-binding natural sample, to steps (2)-(6).

Claims 15-20. (Withdrawn)

Claim 21. (Original) The method according to claims 1, 4, or 5, further comprising, after step (5):

(6) subjecting the reaction mixture resulting from step (5), to at least one structural or functional analysis.

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Claim 22. (Original) The method of claim 21, wherein the at least one analysis in step (6) comprises a member selected from the group consisting of mass spectrometry analysis; liquid chromatography; liquid chromatography coupled on-line with mass spectrometry analysis; infrared spectroscopy; nuclear magnetic resonance; an alternative binding assay; a biochemical assay; a cell-based reporter assay; and an ELISA-based assay.
